Congenital Malformations Registry
Monitoring for Changes in Birth Defects Prevalence

NBDPN 10th Annual Meeting
San Antonio, Texas
February 4-7, 2007

Congenital Malformations Registry Background

Love Canal 1970s

Love Canal Today

- Established October, 1982
- Recognition of the environment as a potential etiologic factor for birth defects (Love Canal)
- Reporting to the Registry is mandated by Public Health Law - State Sanitary Code 22.3

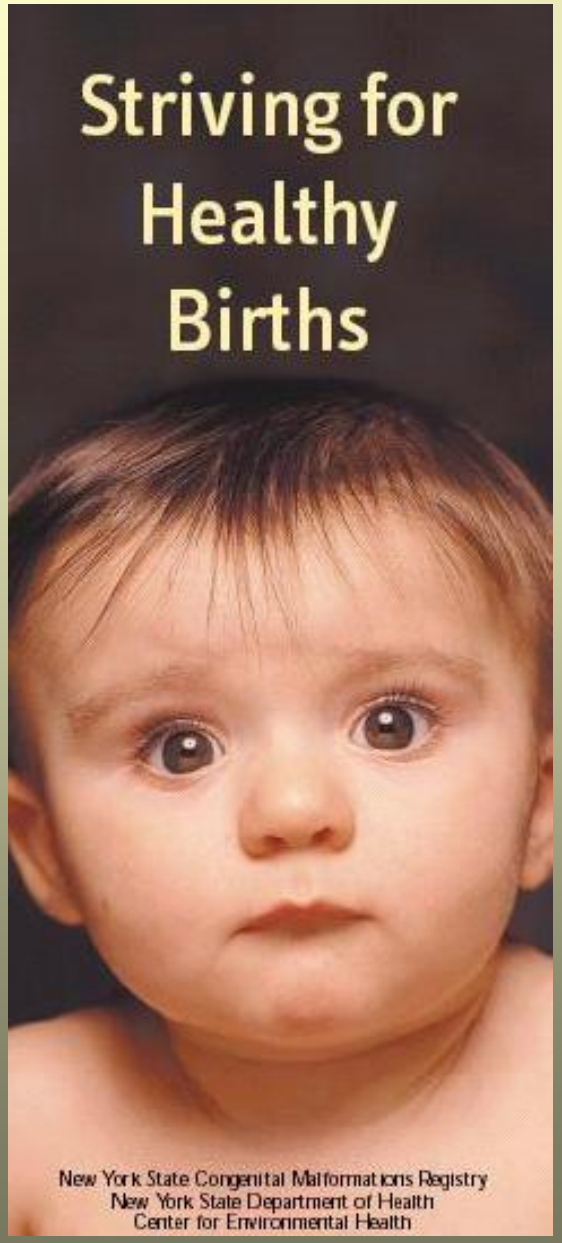
Congenital Malformations Registry Background

Population Coverage: Statewide approximately 260,000 to 300,000 births annually

Designed for surveillance, research & to provide data to health programs to aid in the development of needs assessment

Full time staff - 7.5
Grant funded positions - 12

Congenital Malformations Registry Surveillance System



Registry receives approximately 15,000 electronic reports per year from 165 hospitals statewide on 10,000-11,000 children diagnosed up to the age of 2

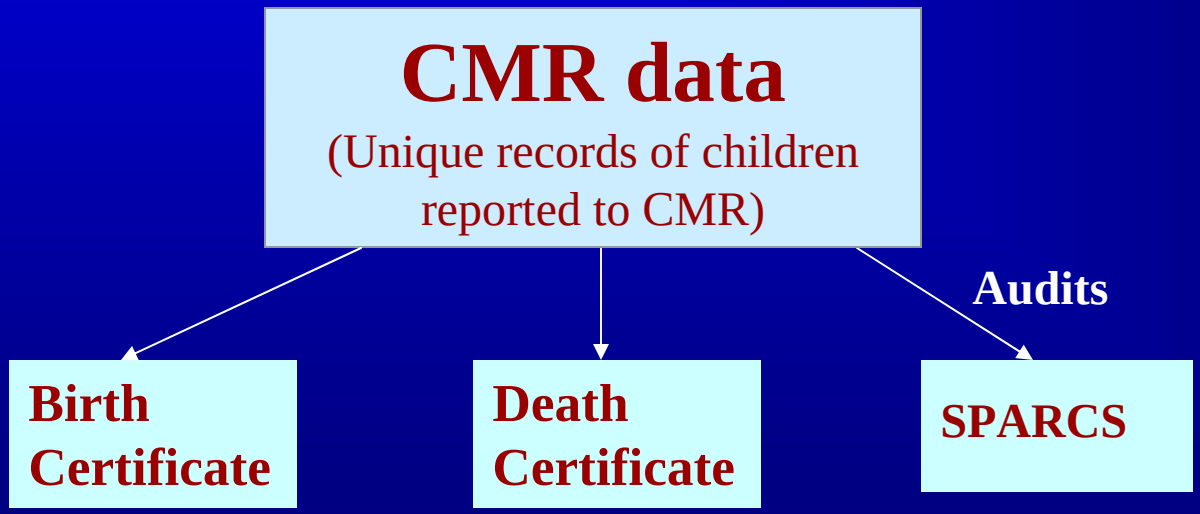
Cases can be diagnosed with 20+ major malformations

Cases can be reported multiple times from one or more hospitals & by physicians

Reports from all sources are maintained and linked with a unique case number

Data Linkage

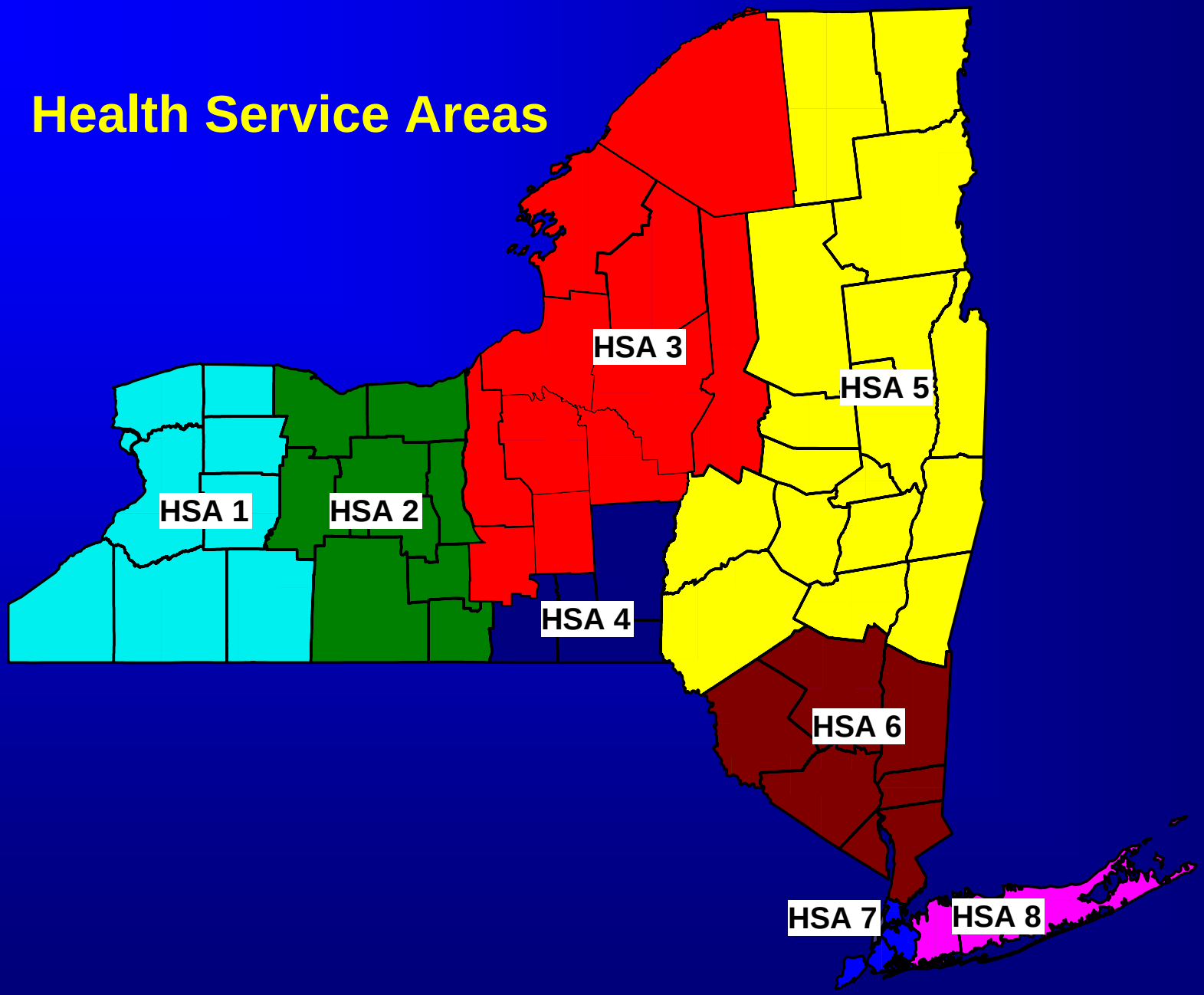
CMR reports are matched with Vital Records & SPARCS hospital discharge files to check the completeness and accuracy of the data and to collect additional variables



CMR Birth Defects Surveillance Previous System

- Performed in January and July
- Analysis by Health Service Areas (HSA) , with HSA 3 & 4 combined due to small number of births
- Compare prevalence of surveillance malformations among infants born in the January to June or July to December time period to same time period for the baseline years

Health Service Areas



Why change to monitoring for variations in space and changes in time & space?

- Mapping and spatial analysis software are readily available and becoming more user friendly
- Increasing availability of geo-referenced environmental and sociodemographic data - State Health Departments
- Can be used as a tool to assess completeness of reporting and detect potential deficiencies
- Additional way to monitor birth defects reporting statewide and to target hospitals for site visits and audits

Why change to monitoring for variations in space and changes in time & space?

- Having procedures in place allows for an informed and quick response to community concerns about possible clusters and environmental exposures

- Small area spatial analysis allows for the investigation of identified geographically localized potential hazards

- Provide guidance for public health interventions

- Ultimate goal of being able to detect significant clusters from a statistical and public health point of view

Caveat *

1a: a warning enjoining one from certain acts or practices
1b: an explanation to prevent misinterpretation

- detecting clustering of birth defects remains a challenge when health events are rare, poorly diagnosed or not adequately reported

- need to avoid generating a multitude of statistically significant results with limited ability to follow-up

- caution should be taken in interpreting maps & results of spatial analysis as errors in registry or vital statistics data could result in erroneous conclusions

* Webster's New Collegiate Dictionary

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Caveats

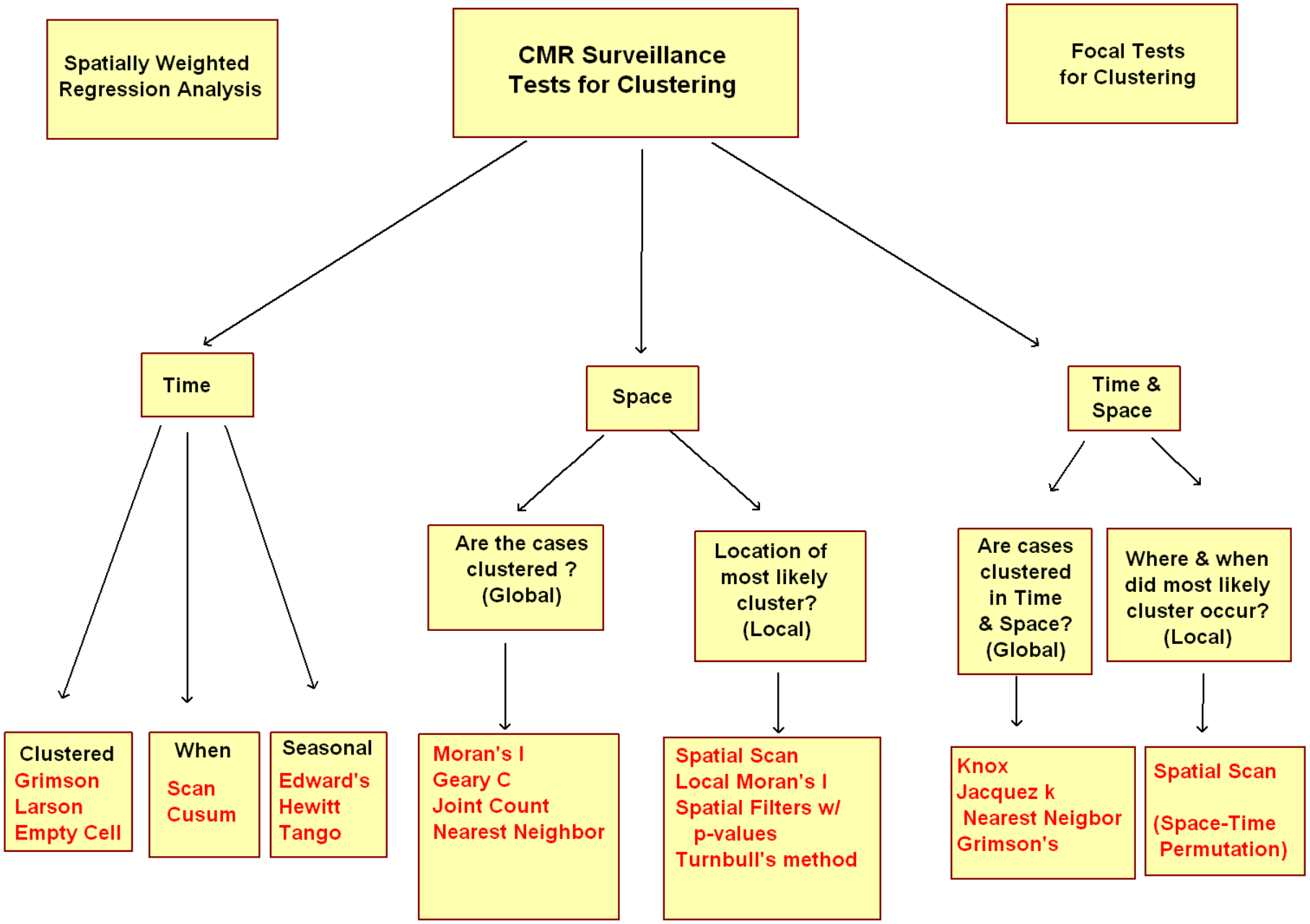
- geographic bias/errors can be introduced through the use of automated geocoding software (Gregorio et al 1999)

- costly and time consuming to accurately geocode large health outcome data sets particularly in rural areas where exact street address information is unavailable

- data collection must ensure that the data are complete and valid

- identification of cause or knowledge about etiology is unlikely to arise from the study of most clusters (Sever, 1994)

- recommend involving experts from various backgrounds to work together to avoid the caveats of GIS (Kirby, 1996)


Spatially Weighted Regression Analysis
CMR Surveillance Tests for Clustering
Focal Tests for Clustering
Time
Space
Time & Space
Clustered
Grimson
Larson
Empty Cell
When
Scan
Cusum
Seasonal
Edward's
Hewitt
Tango
Are the cases clustered ? (Global)
Location of most likely cluster? (Local)
Moran's I
Geary C
Joint Count
Nearest Neighbor
Spatial Scan
Local Moran's I
Spatial Filters w/ p-values
Turnbull's method
Are cases clustered in Time & Space? (Global)
Where & when did most likely cluster occur? (Local)
Knox
Jacquez k
Nearest Neigbor
Grimson's
Spatial Scan
(Space-Time Permutation)

Availability

- SatScan (Spatial Scan; Space-Time Permutation)
- DMap (Spatial filtering)
- CrimeStat (Local Moran's I; Contouring)
- GeoDa (Local Moran's I; Spatially weighted regression)
- Cluster Seer -$$ (24 space time tests)
  - Boundary Seer
  - SpaceStat
- CDC / MACDP developing Automated Spatial Surveillance Project (ASSP)

Environmental Public Health Tracking State Grantees Recommendation to CDC, December 2005

Possible Defects to Monitor

Rank*	malf	malfNo
High	1	01) Anencephalus(BPA=740.x)
High	2	02) Spina Bifida w\o Anencephalus(BPA=741.x)
High	3	03) Encephalocele(BPA=742.0)
High	4	04) Aniridia(BPA=743.42)
High	5	05) Common Truncus(BPA=745.0)
High	6	06) Transposition of Great Arteries(BPA=745.1)
High	7	07) Tetralogy of Fallot(BPA=745.2 & 746.84)
High	8	08) Hypoplastic Left Heart Syndrome(BPA=746.70)
High	9	09) Single/Common ventricle(BPA=745.300)
High	10	10) Cleft Palate w\o Cleft Lip(BPA=749.0)
High	11	11) Cleft Lip w\ & w\o Cleft Lip(BPA=749.1 & 749.2)
High	12	12) Choanal Atresia(BPA=748.0)
High	13	13) Esophageal Atresia/Tracheoesophageal Fistula(BPA=750.3)
High	14	14) Pyloric Stenosis(BPA=750.51)
High	15	15) Renal Agenesis/Hypoplasia(BPA=753.0)
High	16	16) Bladder Exstrophy(BPA=753.50)
High	17	17) Cloacal Exstrophy/persistent cloaca(BPA=751.550)
High	18	18) Hypospadias & Epispadias(BPA=752.6)
High	19	19) Diaphragmatic Hernia(BPA=756.61)
High	20	20) Trisomy 13(BPA=758.1)
High	21	21) Down Syndrome(BPA=758.0)
High	22	22) Trisomy 18(BPA=758.2)
Medium/High	23	23) Anotia/Microtia(BPA=744.01 & 744.21)
Medium/High	24	24) Endocardial Cushion Defect(BPA=745.6)
Medium/High	25	25) Ebsteins Anomaly(BPA=746.20)
Medium/High	26	26) Rectal & Large Intestinal Atresia/Stenosis(BPA=751.2)
Medium/High	27	27) Reduction Deformity, Upper Limbs(BPA=755.2)
Medium/High	28	28) Reduction Deformity, Lower Limbs(BPA=755.3)
Medium/High	29	29) Sacral agenesis(BPA=756.170)
Medium	30	30) Hydrocephalus w\o Spina Bifida(BPA=742.3)
Medium	31	31) Microcephalus(BPA=742.10)
Medium	32	32) Anophthalmia/Microphthalmia(BPA=743.00-743.10)
Medium	33	33) Congenital Cataract(BPA=743.32)
Medium	34	34) Atrial Septal Defect(BPA=745.51-745.59)
Medium	35	35) Tricuspid Valve Atresia & Stenosis(BPA=746.10)
Medium	36	36) Aortic Valve Stenosis(BPA=746.30)
Medium	37	37) Coarctation of Aorta(BPA=747.1)

Defects to Monitor – Additional Considerations

- **monitor for the occurrence of various grouped defects (pathogenetically similar) defects to increase power e.g. NTDs**
- **monitor for multiple malformations excluding specific sequences**
- **monitor for selected multiple malformation combinations**
- **monitor occurrence of surveillance defects as isolated or in combination with other defects (e.g. cleft lip vs. cleft lip with Trisomy 13)**
- **groups to monitor based on embryology ?**

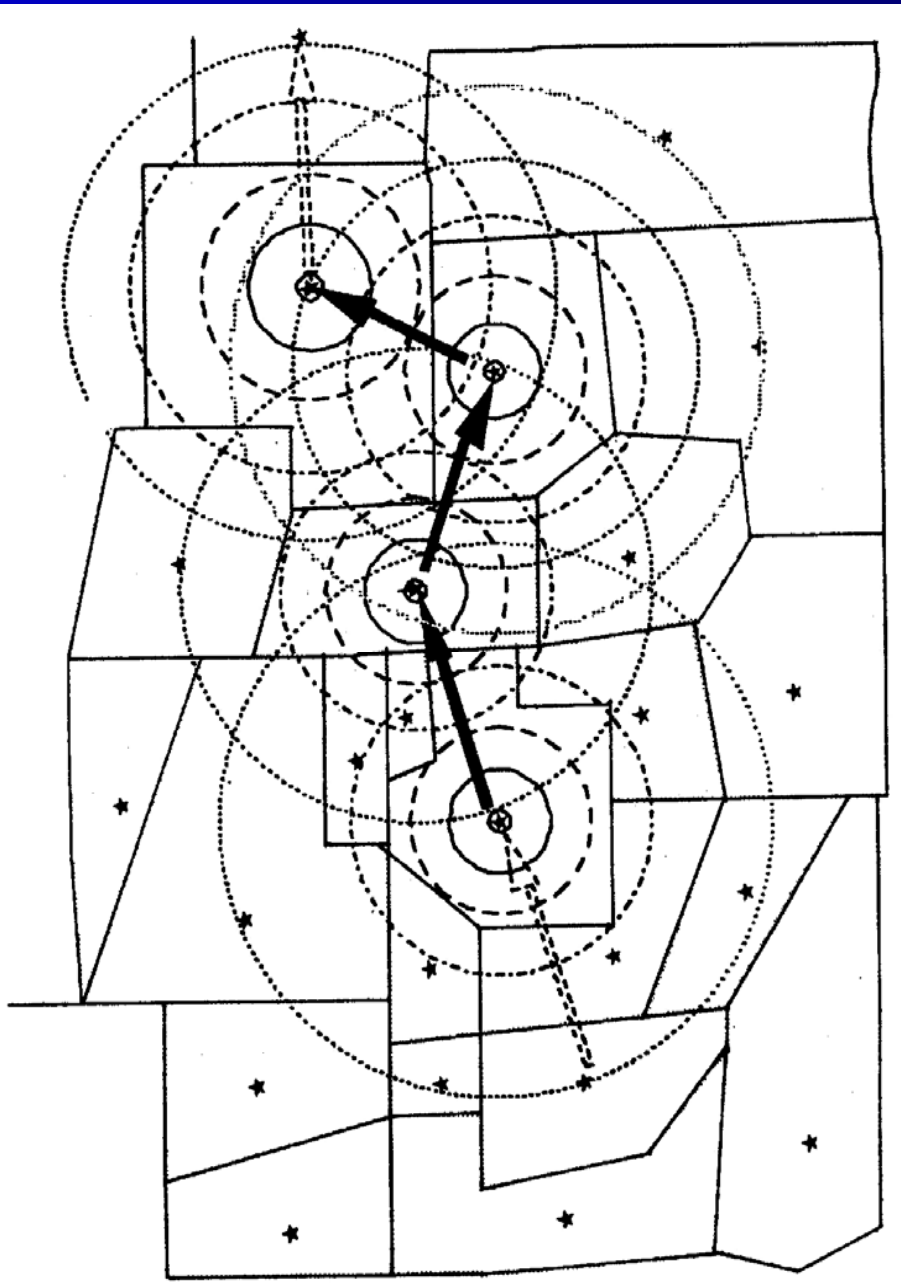
Spatial Scan Statistic

- Circular search “window’ is positioned on centroid of each ZIP code and expanded to a pre-defined limit

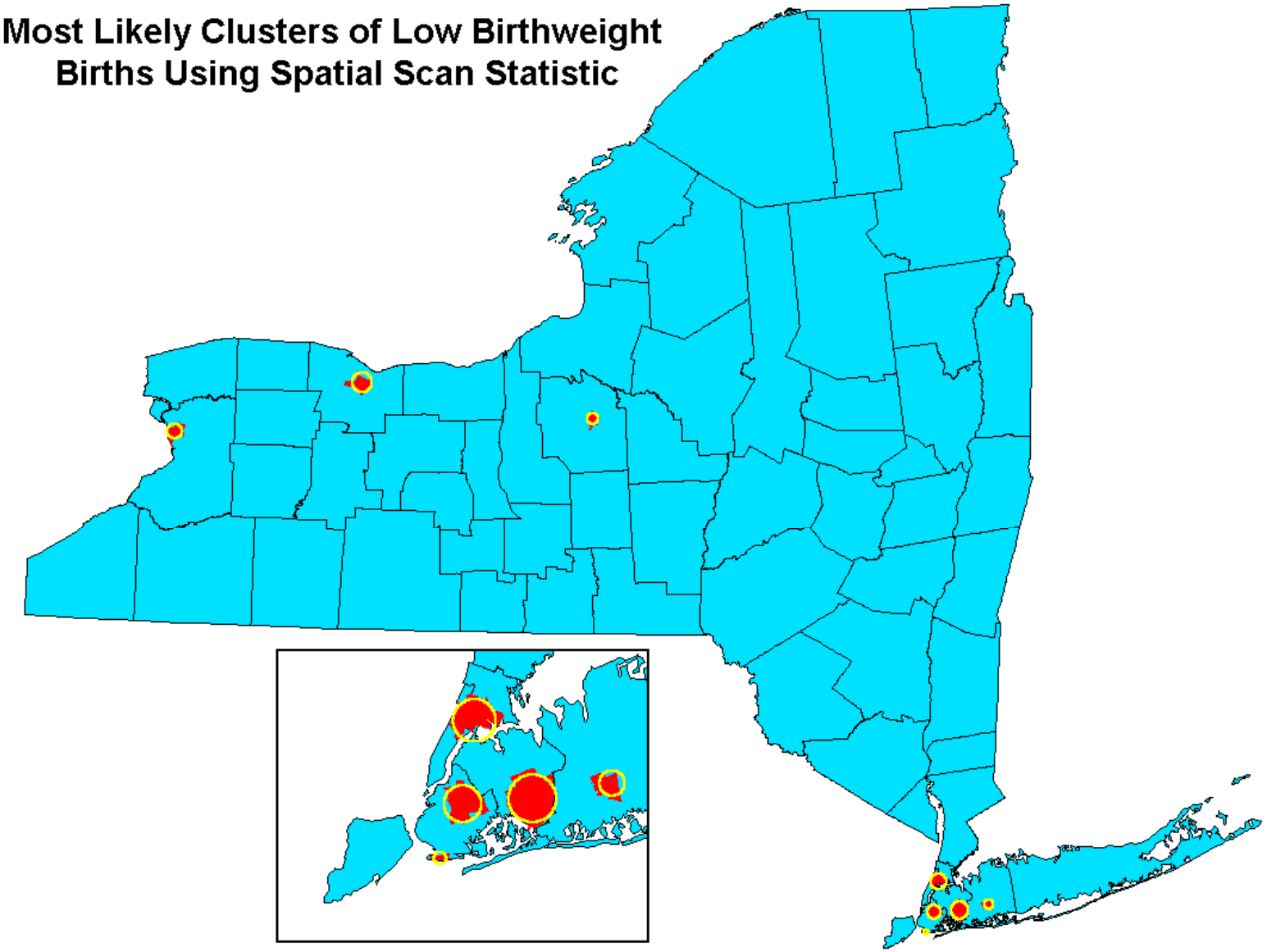
  (%5 of all births)

- For each window , the likelihood ratio of finding the observed number of cases, relative to number of births, inside and outside the circle is compared.

- Statistical significance determined through Monte Carlo testing

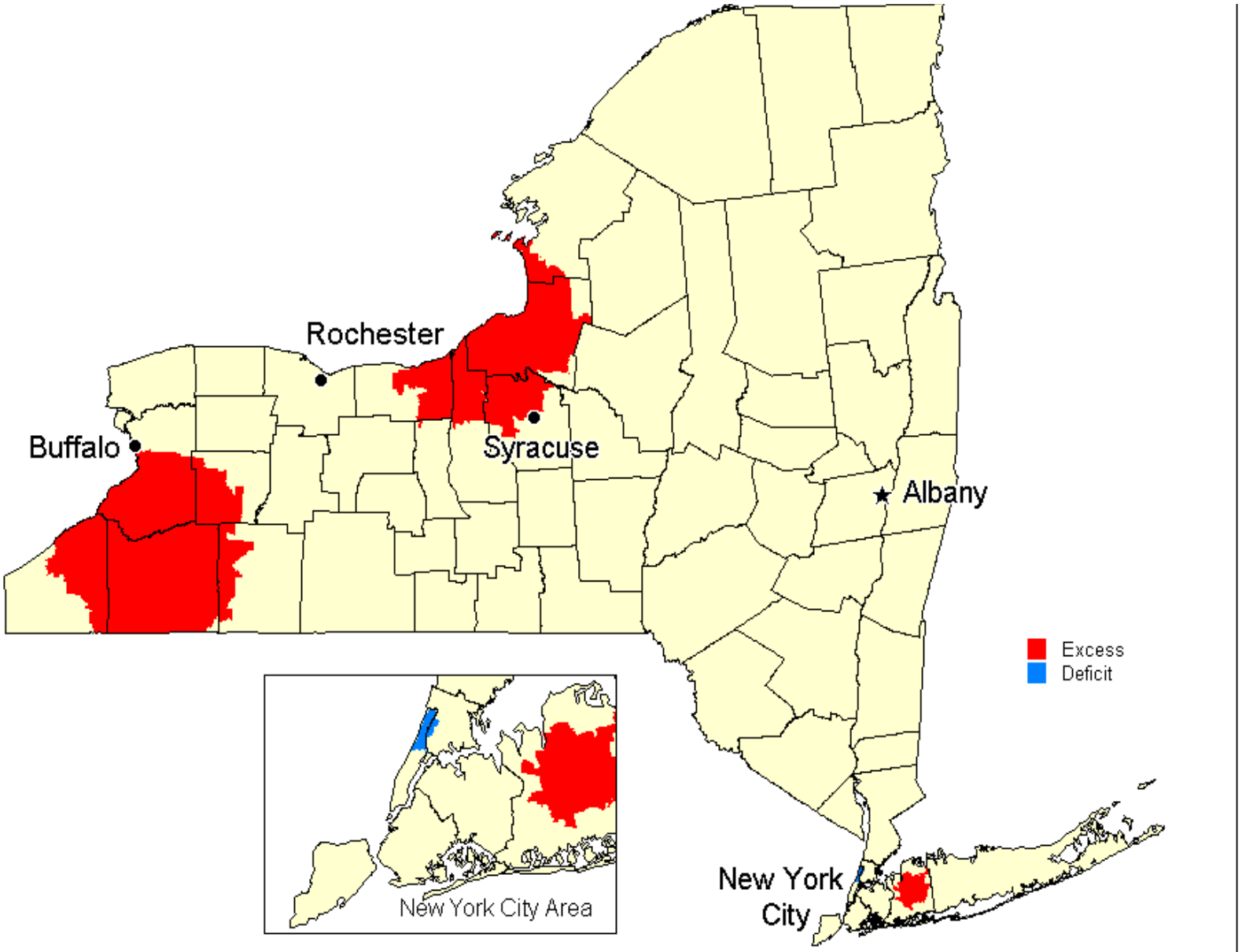


Most Likely Clusters of Low Birthweight Births Using Spatial Scan Statistic



p<0.05 Restictions; no cluster can contain more than 10% of births.

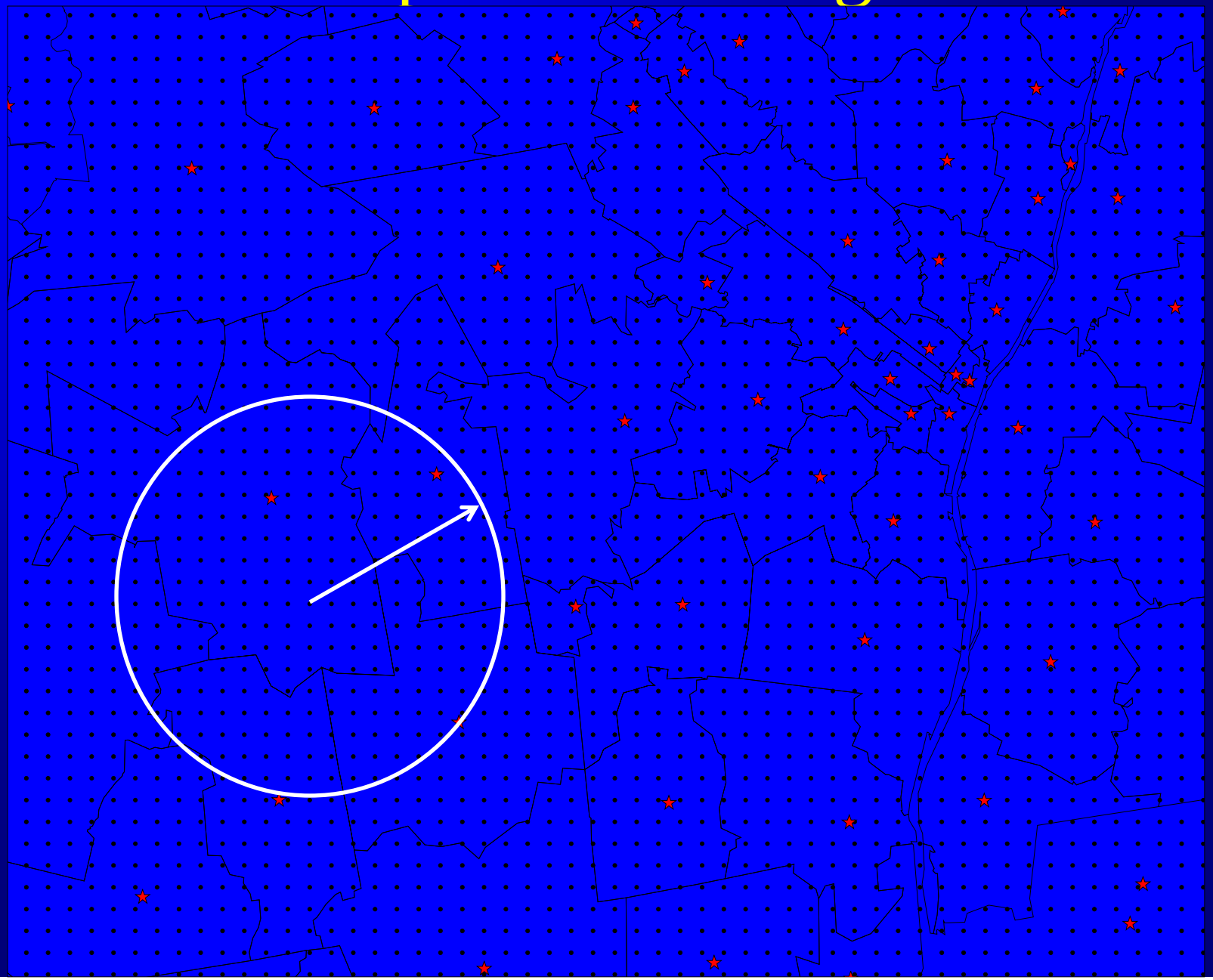
Congenital malformations clusters identified using the scan statistic at p<.05 in NYS, 1992-1995

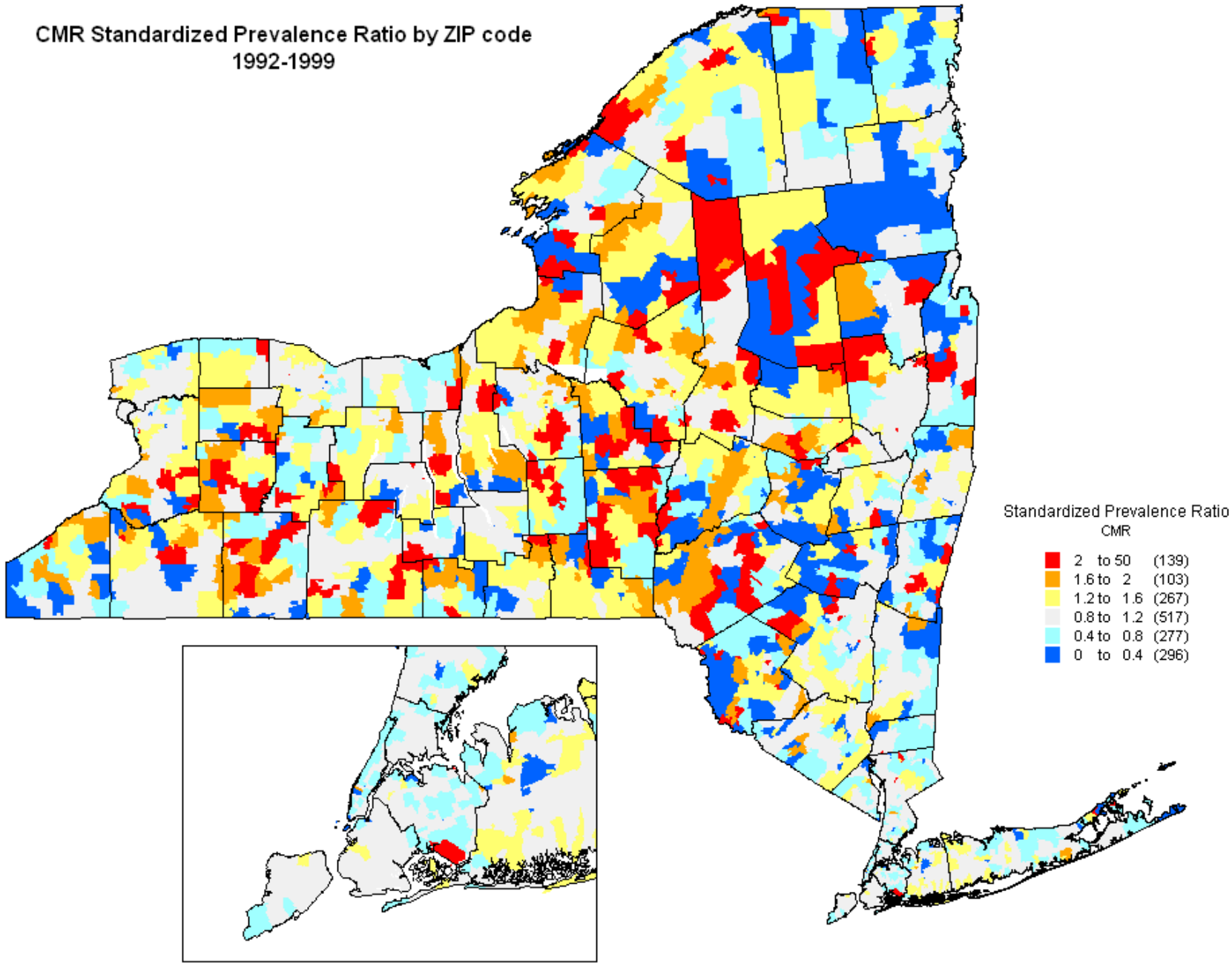


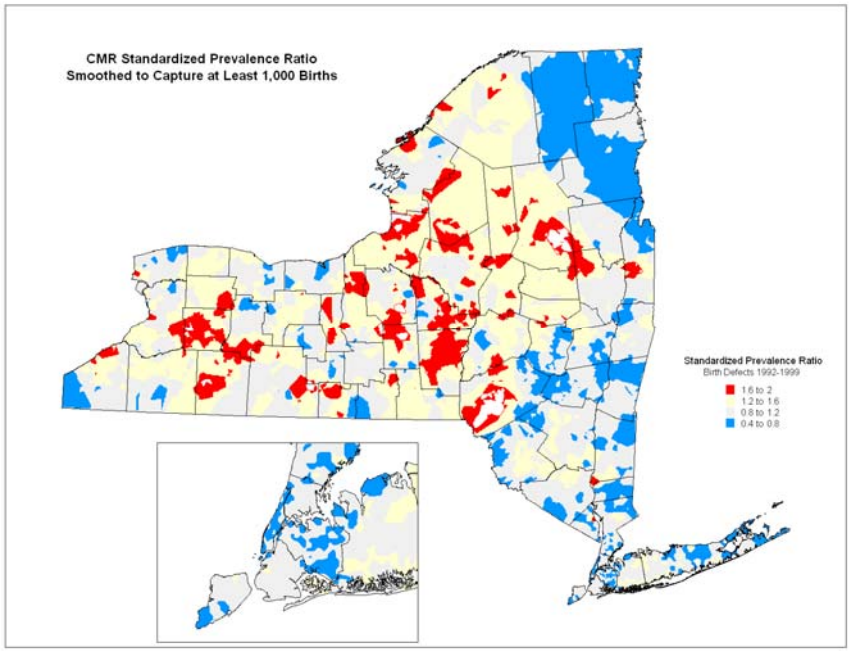
Spatial Filters

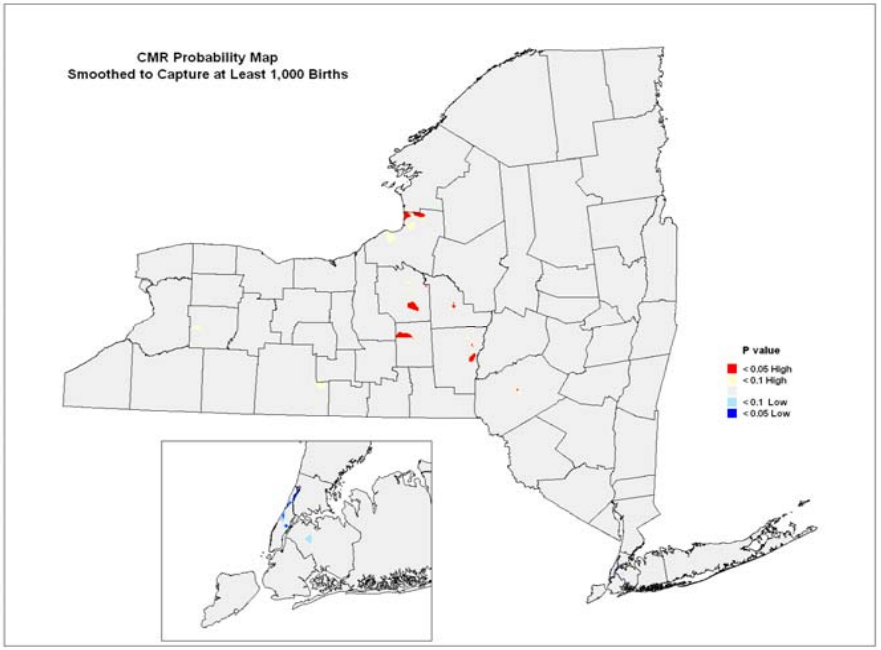
- Population based spatial smoothing method
- Can be used on individual and group level data
- Simultaneously computes rates and p-values using MLR and Monte Carlo simulations to identify significantly elevated areas.
- Used at multiple resolutions (population size)

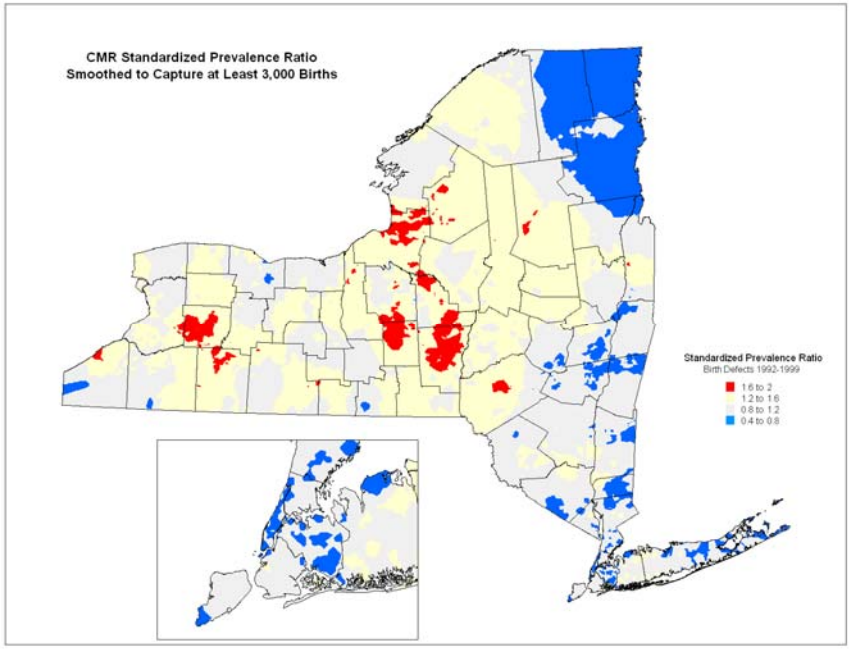
Spatial Filtering

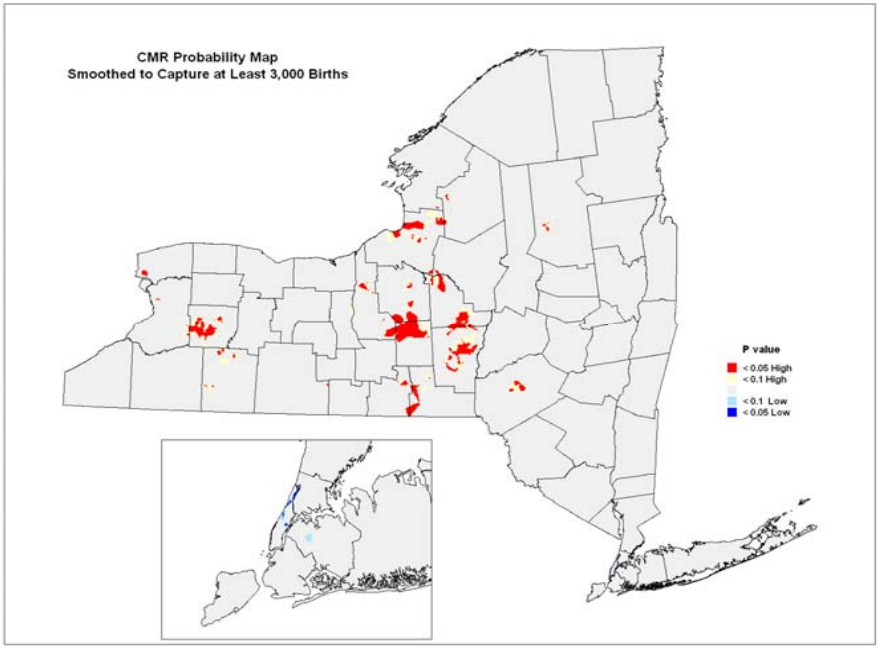



CMR Standardized Prevalence Ratio by ZIP code
1992-1999
Standardized Prevalence Ratio
CMR
2 to 50 (139)
1.6 to 2 (103)
1.2 to 1.6 (267)
0.8 to 1.2 (517)
0.4 to 0.8 (277)
0 to 0.4 (296)


CMR Standardized Prevalence Ratio
Smoothed to Capture at Least 1,000 Births
Standardized Prevalence Ratio
Birth Defects 1992-1999
1.6 to 2
1.2 to 1.6
0.8 to 1.2
0.4 to 0.8


CMR Probability Map
Smoothed to Capture at Least 1,000 Births
P value
< 0.05 High
< 0.1 High
< 0.1 Low
< 0.05 Low


CMR Standardized Prevalence Ratio
Smoothed to Capture at Least 3,000 Births
Standardized Prevalence Ratio
Birth Defects 1992-1999
1.6 to 2
1.2 to 1.6
0.8 to 1.2
0.4 to 0.8

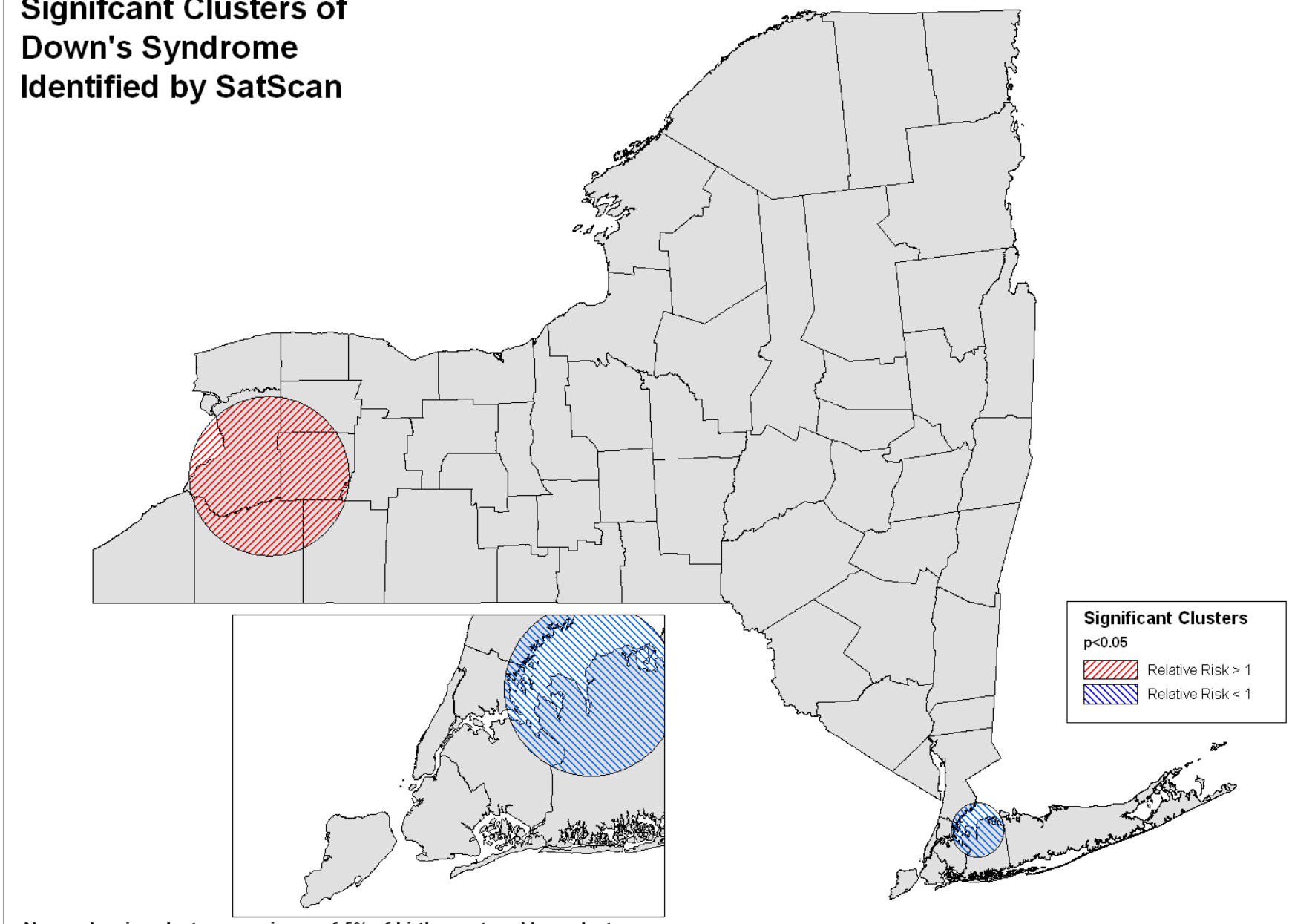

CMR Probability Map
Smoothed to Capture at Least 3,000 Births
P value
< 0.05 High
< 0.1 High
< 0.1 Low
< 0.05 Low

Local Cluster Tests

- Turnbull's method
- Besag and Newell's method

- Both use group level data (#cases/births)
- A circular window is centered on each region and expand outward until:
  - Minimum population size met (Turnbull)
  - Minimum number of cases met (Besag-Newell)
- Compare rate inside vs. outside circle
- Use Monte Carlo simulations to test for significance

Signifcant Clusters of Down's Syndrome Identified by SatScan



No overlapping clusters; maximum of 5% of births captured by a cluster

SatScan Log for Downs Syndrome
Western and Central NYS

Purely Spatial analysis
scanning for clusters with
high or low rates using the Poisson model.

SUMMARY OF DATA

Number of ZIP Codes: 548
Total population .....: 442,935
Total cases .....: 456
Annual cases / 10,000.: 10.3

MOST LIKELY CLUSTER

ZIP Codes included.: 14001
Coordinates / radius..: (43.0438 N, 78.4965 W) / 0.00 km
Births.....: 835
Number of cases.....: 5 (0.86 expected)
Overall relative risk.: 5.8
Log likelihood ratio..: 4.7
Monte Carlo rank.....: 9,685/10,000
P-value.....: 0.9685

Recommendations

- Evaluate the results of several clustering programs and compare and contrast the results
- Check data quality by region to assure consistency across the state
- To investigate clusters around a putative source of pollution use a focused test.
- Cluster detection methods are most suitable for exploratory data analysis(hypothesis generating)
  - Once hypotheses have been generated they need to be tested with more formal epidemiological studies

Recommendations

- Many time-space clusters will be due to chance and care must be taken in selecting which alarms to follow-up
- Consideration given to not only to statistical significance but to the absolute number of events
- To investigate a "significant" cluster recommend following methodology similar to that outlined by the CBDMP (Harris et. al., 1999) also a NCBDDD paper in Teratology by (Williams et.al., 2002)
- Recommend article by Siffel et. al. 2006 in Birth Defects Research Part A-describes role of GIS in birth defects surveillance & research

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